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Topical permethrin exposure inhibits antibody production and macrophage function in C57Bl/6N mice.

Punareewattana K, Smith BJ, Blaylock BL, Longstreth J, Snodgrass HL, Gogal RM Jr, Prater RM, Holladay SD.

Department of Biomedical Sciences and Pathobiology, Virginia-Maryland College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061-0442, USA.

Permethrin was applied to the shaved dorsal interscapular region of C57Bl/6N mice at doses of 0.5, 1.5 or 5.0 microl/day. These doses corresponded to approximately 22-220 mg/kg/day topical insecticide. Mice were exposed to permethrin in this manner daily for 10 or 30 consecutive days, or every other day for 7 or 14 exposures. The splenic macrophage chemiluminescent response was depressed in a dose-dependent manner at 2 and 10 days post-exposure to permethrin. Phagocytic ability of macrophages was not inhibited. Antibody production as shown by plaque-forming cell (PFC) assay decreased significantly after 10 consecutive days of exposure to permethrin. These data indicate that topical permethrin exposure may produce systemic immune effects.

PMID: 11267706 [PubMed - indexed for MEDLINE]

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Malnutrition, Urocanic Acid, and Sun May Interact to Suppress Immunity in Sojourners to High Altitude

Daniel H. Hug, Ph.D., John K. Hunter, M.A., and Duane D. Dunkerson, M.A.
Aviat Space Environ Med 2001; 72:136-45

Abstract

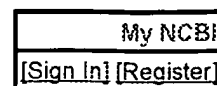
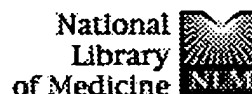
Irradiation of skin by ultraviolet radiation in mice and humans leads to a suppression of cell-mediated immunity. This process is initiated when one of the photoreceptors in skin, *trans*-urocanic acid, is photoisomerized to *cis*-urocanic acid, an immunomodulator. High levels of L-histidine, histamine, and *trans*-urocanic acid are found in humans and animals when they are protein malnourished. Mice fed on an elevated L-histidine diet have more *trans*-urocanic acid in the skin and are more susceptible to UV-induced immune suppression. Sojourners to high altitudes are malnourished, suffer protein catabolism, are exposed to sun, and often acquire infectious diseases. There is evidence that sunscreens may not adequately protect the immune system. Furthermore, UV intensity increases with altitude. We propose a testable hypothesis: UV radiation causes photoimmune suppression in sojourners to high altitude and this allows infectious diseases to develop. The mechanism we propose includes protein malnutrition, high levels of *trans*-urocanic acid, ultraviolet radiation, formation of *cis*-urocanic acid, immune suppression, and infection.

Keywords: high altitude, photoimmune suppression, urocanic acid, protein malnutrition.

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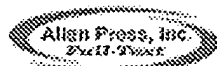
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Suppression of different phases of systemic contact hypersensitivity by urocanic acid oxidation products.

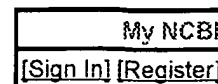
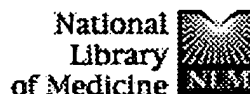
Kammeyer A, Garssen J, Sleijffers A, van Loveren H, Eggelte TA, Bos JD, Teunissen MB.

Department of Dermatology, Academic Medical Center, University of Amsterdam, PO Box 22700, NL-1100 DE Amsterdam, The Netherlands.
a.kammeyer@amc.uva.nl

On exposure to UV-B, the epidermal component trans-urocanic acid (UCA) is not only photoisomerized into cis-UCA but will also, at least in part, be photooxidized into UCA oxidation products (UOPs). We hypothesized that UOPs can mimic UV-induced systemic immunosuppression comparable to the suppressive properties already established for cis-UCA. A crude mixture of UOPs showed a significant suppression of the sensitization phase of the systemic contact hypersensitivity (CHS) response to picryl chloride (PCI). Three of the UOPs were selected for this study: imidazole-4-carboxylic acid (ImCOOH), imidazole-4-carboxaldehyde (ImCHO) and imidazole-4-acetic acid (ImAc). Effects on the sensitization, elicitation and postelicitation phases of CHS to PCI in BALB/c mice were studied and compared with the effects of cis-UCA. ImCHO was equally effective at suppressing the sensitization phase as cis-UCA. The triplet combination of the imidazoles (1:1:1) showed more pronounced suppression than that induced by cis-UCA. The most effective compounds for the suppression of the elicitation phase appeared to be ImAc and cis-UCA. Significant suppression of the postelicitation phase was only obtained with the triplet combination of ImCHO, ImCOOH and ImAc, the combination that appeared to be effective at all three tested phases. Because these three UOPs are present in UV-B-exposed human stratum corneum, these compounds may play a role in UV-B-induced immunosuppression.

PMID: 15339212 [PubMed - indexed for MEDLINE]

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1: Photochem Photobiol. 1997 Mar;65(3):593-8.

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Prolonged increase of cis-urocanic acid levels in human skin and urine after single total-body ultraviolet exposures.

Kammeyer A, Pavel S, Asghar SS, Bos JD, Teunissen MB.

Department of Dermatology, University of Amsterdam, The Netherlands, A.Kammeyer@AMC.UVA.NL

Cis-urocanic acid (cis-UCA), a mediator of immunosuppression, is formed from trans-UCA upon UV-exposure of the skin. This study describes a liquid chromatographic method for the simultaneous quantification of cis- and trans-UCA in skin, urine and plasma of nonirradiated volunteers. It also describes cis- and trans-UCA kinetics in UV-irradiated volunteers. New procedures to remove interfering substances from urine and plasma are reported. Normal levels of cis-UCA in skin, urine and plasma of nonirradiated volunteers were 0.5 nmol/cm², 0.03 μmol/mmol creatinine (median 0.00) and undetectable and those of trans-UCA were 17.1 nmol/cm², 1.36 μmol/mmol creatinine and 0.5 μM, respectively. Upon single total body UVB (290-320 nm) exposures of 250 J/m², epidermal cis-UCA levels immediately reached a maximum and returned to basic levels 3 weeks later. The cis-UCA levels in urine reached a maximum in 5-12 h postirradiation and reached baseline values in 8-12 days. Additionally, a single total body UVA (320-400 nm) irradiation of 200 kJ/m² yielded a similar pattern. The kinetics of cis-UCA in plasma could not be followed due to low concentrations; however, that of skin and urine was informative in relation to solar exposures and phototherapy.

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